2020

Is Virtual Reality Training Effective In Improving The Quality Of Life For Adults With Parkinson's Disease?

Judy Le
Philadelphia College of Osteopathic Medicine

Is Virtual Reality Training Effective In Improving The Quality Of Life For Adults With Parkinson's Disease?

Judy Le, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 13, 2019

ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not virtual reality training is effective in improving the quality of life for adults with Parkinson's disease.

STUDY DESIGN: A systematic review of two randomized controlled trials (RCTs) and one case series published between the years of 2017 and 2018.

DATA SOURCES: All articles were published in English and were taken from peer-reviewed journals using CINAHL Plus. All articles were selected based on relevance to clinical question, evaluation of patient-oriented outcomes, and date of publication.

OUTCOMES MEASURED: Each of the three articles analyzed the effects of virtual reality training on improving quality of life (QOL) for adults with Parkinson's disease. The Parkinson's Disease Questionnaire-39 (PDQ-39) and Parkinson's Disease Questionnaire-8 (PDQ-8) were used to measure quality of life, which were reported as mean change from baseline.

RESULTS: In the RCT conducted by Tollar et al., (*J Cent Nerv Syst Dis*. 2018;10: 1179573518813541. doi:10.1177/1179573518813541) researchers found that PDQ-39 scores did improve following virtual reality rehabilitation ($p<0.001$). In the RCT by Gandolfi et al., *(Arch Phys Med Rehabil*. 2018;99(12):247-2484.e1. doi: //doi.org/10.1016/j.apmr.2018.05.007.) there was also significant improvement in the PDQ-8 scores before and after the intervention of virtual reality training ($p<0.001$). However, the case series performed by Souza et al. (*Fisioterapia em Movimento*. 2018;31. doi:10.1590/1980-5918.031.ao12.) showed insignificant findings in the overall PDQ-39 scores after the intervention was implemented ($p=0.135$).

CONCLUSIONS: The three studies evaluated in this review provided inconclusive evidence on whether or not virtual reality training is effective in improving quality of life for adults with Parkinson's disease. Tollar et al. (*J Cent Nerv Syst Dis*. 2018;10: 1179573518813541. doi:10.1177/1179573518813541) and Gandolfi et al. *(Archives of Physical Medicine and Rehabilitation*. 2018;99(12):247-2484.e1. doi: //doi.org/10.1016/j.apmr.2018.05.007.) demonstrated a statistically significant improvement in quality of life whereas Souza et al. (*Fisioterapia em Movimento*. 2018;31. doi:10.1590/1980-5918.031.ao12.) showed no significance. Due to the conflicting results and limitations mentioned in each study, further investigation is warranted to more effectively evaluate the effects of virtual reality rehabilitation in improving quality of life for adults with Parkinson's disease.

KEY WORDS: Parkinson's, virtual reality, physical therapy

INTRODUCTION

Parkinson's disease is a progressive neurodegenerative disorder that occurs due to deterioration of dopamine in the substantia nigra and degeneration of the basal ganglia, which leads to a loss in control of voluntary movements. Although Parkinson's disease has conventionally been identified as a type of movement disorder, it is now considered a complex disorder with additional neuropsychiatric and nonmotor manifestations.[1] The progressive decline of motor and cognitive functions can consequently result in adverse effects on an individual's independence and quality of life (QOL).[2]

As the second most-common neurodegenerative disorder in the US, the prevalence of Parkinson's disease in the US is 0.3% in the general population, 1-2% in persons over age 65, and 4-5% in persons over age 85.[1] The national economic burden of this condition is estimated to be above $14.4 billion with the cost at approximately $22,800 per patient.[1] In 2010, the population of Parkinson's disease patients incurred nearly 1.9 million hospital inpatient days and 1.26 million physician office visits.[1] As the number of people living with neurological conditions like Parkinson's disease steadily rises with age, it is projected that the burden of the disease will grow with the aging population.

It is well understood that the signs and symptoms of Parkinson's disease are predominately due to the loss of dopaminergic neurons in the midbrain. This disease is characterized primarily by motor impairments including resting tremor, bradykinesia, rigidity, and abnormal gait. Nonmotor clinical manifestations include, but are not limited to, cognitive changes, psychosis, depression, anxiety, sleep disturbances, autonomic dysfunction, olfactory issues, and gastrointestinal disturbances. As the diverse clinical features of the disease can vary greatly between patients, it is important for healthcare clinicians to recognize the characteristic

signs and symptoms in order to properly diagnose the condition and provide symptomatic treatment early on to prevent mobility-related disability and comorbidities.[3]

While it is it is believed that Parkinson's disease is a multifactorial neurodegenerative process that occurs from a combination of factors such as aging, neuronal susceptibility, genetic predisposition, and environmental exposures, the exact cause of disease is unknown.[4] With that being said, there is no standard treatment approach for patients.[1] Nearly all available treatments can provide symptomatic relief, however these interventions do not reverse the effects of the disease. As mid-level practitioners, physician assistants working in the hospital and outpatient setting must integrate various treatment modalities into their plan of care to help relieve symptoms and maintain quality of life for patients.

Management of this condition with nonpharmacologic, pharmacologic, and/or surgical therapy must be personalized to the needs of the individual patient. Non-pharmacologic intervention involves lifestyle management with exercise, diet modifications, use of assisted walking devices, speech therapy, and occupational therapy. Pharmacologic therapy is considered the first-line treatment option for PD, which includes levodopa, dopamine agonists, MAO-B inhibitors, and amantadine.[4] Surgical options, such as pallidotomy and deep brain stimulation, can be utilized in advanced disease refractory to pharmacological treatment.[4]

As mentioned previously, Parkinson's disease patients can suffer from motor impairments, such as postural instability and gait disturbances, which can adversely affect their level of independence and quality of life.[6] As postural instability is known to be refractory to medications, rehabilitation is especially valuable in the management of Parkinson's disease.[3] Virtual reality therapy is an innovative approach to rehabilitation that is aided by gaming technology in order to provide multisensory and complex exercise stimuli to participants. This

therapy allows patients to engage in virtual reality scenarios by using their body movements to control and play video games, which has been proven to be feasible and effective in neurological conditions.[3] It is thought that virtual reality training can help improve the quality of life for Parkinson's disease patients by promoting positive effects on posture and gait.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not "Is virtual reality training effective in improving the quality of life for adults with Parkinson's disease?"

METHODS

The articles utilized for this systematic review were found online via CINAHL Plus by using the following key words: Parkinson's, virtual reality, and physical therapy. Each study was published in English in a peer-reviewed journal between the years of 2017 and 2018. These sources were selected based on their relevance to the clinical question and evaluation of patient-oriented outcomes (POEMs). Inclusion criteria for the studies included studies published after 2016. Exclusion criteria for the studies included studies published in 2016 or earlier. Summary of statistics used in this review to determine clinical significance include p-value and mean change from baseline.

The data sources of this systematic review specifically focused on the population of adults with Parkinson's disease. The three studies that were utilized for this review include two randomized controlled trials (RCTs) and one case series. Each RCT compared the intervention group of virtual reality training to two different control groups: no physical intervention and in-clinic balance training. The case series did not compare the intervention to any control group. The outcome that was measured in all three studies was quality of life.

Table 1. Demographics and Characteristics of Included Studies

Study	Type	# of Pts	Age	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Souza[2] (2018)	Case Series	11	65 ±9.6	Patients with modified Hoehn and Yahr stages 1-3, normal or corrected visual and auditory acuity, no previous involvement with Kinect system, and no involvement in an exercise program within last 2 months.	Patients who presented with any type of clinical deficit that made it difficult to perform standing exercises like cardiorespiratory, orthopedic, or neurological problems.	0	Virtual reality using Xbox Kinect Adventures.
Gandolfi[3] (2017)	RCT	76	67.45 ±7.18	Patients >18 years old, modified Hoehn and Yahr stages 2.5-3, steady medication usage in last month, ability to perform postural transfer and ability to remain standing posture for 10 minutes, and presence of caregiver.	Patients with cardiovascular, orthopedic, otovestibular disorders, visual or neurological disorders, severe dyskinesia, severe on-off fluctuations, MMSE score <24/30, or depression.	6	Home-based virtual reality tele-rehabilitation vs. in-clinic sensory integration balance training.
Tollar[6] (2018)	RCT	72	67.6 ±3.4	Patients with Hoehn and Yahr stages 2-3 who are currently taking Levodopa equivalent medications.	Patients with cognitive deficits, depression, severe cardiovascular disease, uncontrolled DM, history of stroke, traumatic brain injury, seizure disorder, or current involvement in an exercise program.	9	Virtual reality training using XboxTM vs. no physical intervention.

OUTCOMES MEASURED

The patient-oriented outcome that was measured in each article was quality of life. Souza et al. used the Parkinson Disease Questionnaire-39 (PDQ-39), a self-reported survey of 39 questions that assessed 8 domains: mobility, daily life activities, emotional state, stigma, social support, cognition, communication, and body discomfort. Each domain was scored from 0 to 100, with a lower score representing a better perception of quality of life. Each participant completed the PDQ-39 before treatment, immediately after treatment, and 30 days after treatment, which was presented as mean differences before and after treatment. Tollar et al. also utilized the PDQ-39 to measure quality of life scores in both groups before and after treatment. The results of the PDQ-39 were reported as mean differences, with a change of 4.7 considered as clinically significant.[6] Gandolfi et al. used the Parkinson Disease Questionnaire-8 (PDQ-8) to measure quality of life. The participants of this study completed the self-reported survey before treatment, after treatment, and 1 month following treatment. The quality of life scores, presented as mean values, were compared between the tele-rehabilitation group and the in-clinic rehabilitation group, and also within each group overtime.

RESULTS

The case series performed by Souza et al. consisted of 11 participants between the ages of 48 to 76 years old, who had a diagnosis of Parkinson's disease with stage 1 to 3 classification on the Hoehn and Yahr Scale.[2] This study, completed at the University of Sao Paulo in Brazil, selected participants based on convenience for the study and inclusion criteria of normal or corrected visual and auditory acuity, no previous involvement with Kinect system, and no involvement in an exercise program within the last 2 months. Participants were excluded if they presented with any cardiorespiratory, orthopedic, or other detectable neurologic disability, such

as dementia or clinical signs of dyskinesia, due to the possibility that any clinical impairments from these conditions might have negatively affected their ability to perform standing exercises.

In this study by Souza et al., each subject participated in a total of 14 one-hour sessions (twice a week for 7 weeks) where they played 4 different games of Kinect Adventures on a virtual-reality system via a X-Box gaming device.[2] The games, selected based on motor and cognitive demands, were completed 5 times with assistance by a physiotherapist. Patients were not involved in any other type of rehabilitation during the period of the study. There were no reports on safety, tolerability, or adverse effects of treatment.

The PDQ-39 assessed quality of life by evaluating the mean scores of 8 different domains pre- and post- treatment with a p-value of <0.05 considered to be clinically significant.[2] As presented in Table 2, the only domain that demonstrated a substantial improvement was the activities of daily living, in which there was a significant decrease of 8.7 in the pre-treatment score to the 30-day post-treatment score ($p<0.023$).[2] This improvement in daily activities was attributed to the enhancement of postural control and cognition with the virtual reality games.[2] The other seven domains plus the total PDQ-39 score demonstrated no significant change in mean values pre- and post-treatment ($p>0.05$).[2] Based on the results for all of the domains, besides daily activities, the mean difference was lower than the value defined by the author.

Table 2. Mean (SD) Change in QOL and P-Values in a Study Conducted by Souza et al.[2]

Domain	Pre-Intervention Mean (SD)	30 Days Post-Intervention Mean (SD)	P-Value
Mobility	23.9 (27.5)	10.9 (9.6)	0.328
Activities of Daily Living*	29.9 (22.7)	21.2 (21.8)	0.023
Emotional Well Being	22.0 (22.8)	21.2 (15.0)	0.794
Stigma	10.2 (15.6)	11.9 (17.3)	0.692
Social Support	65.2 (5.0)	68.9 (5.4)	0.135
Cognition	21.0 (13.8)	18.2 (15.9)	0.248
Communication	22.7 (25.8)	18.2 (21.0)	0.446
Body Discomfort	30.3 (23.9)	34.8 (25.8)	0.682
Total	27.0 (11.9)	21.8 (8.2)	0.135
*P-value <0.05 is significant			

The multisite, single-blind RCT completed by Gandolfi et al. involved patients with Parkinson's disease and modified Hoehn and Yahr stages 2.5-3.[3] Initially, there were 135 outpatients at 4 different neurorehabilitation units located in Veneto who were assessed for eligibility. Inclusion criteria to participate included age >18 years old, modified Hoehn and Yahr stages of 2.5-3, steady medication usage in last month, ability to perform postural transfer and ability to remain standing posture for 10 minutes, and presence of a caregiver. Patients were excluded if they had any cardiovascular, orthopedic, or otovestibular disorders; visual or neurological disorders; severe dyskinesia or severe on-off fluctuations; Mini Mental State Examination score <24/30; or depression. Of the original 135 patients, 26 patients were excluded due to criteria stated above, 13 declined to participate, and 20 faced technological issues preventing their participation.

The remaining 76 subjects in the study conducted by Gandolfi et al. were randomly assigned by a computer-generated random number table into either the in-home virtual reality tele-rehabilitation (TeleWii) group or the in-clinic sensory integration balance training (SIBT) group.[3] Two patients in the TeleWii group and four patients in the SIBT group withdrew from the study due to medical reasons or transportation issues. Both groups participated in 21 sessions of 50-minute rehabilitation. The TeleWii group consisted of balance exercises using the Nintendo Wii Fit System, which was supervised by a physiotherapist. Under instruction and support of a physical therapist, the SIBT group participated in 10 exercises aimed at improving postural stability. Patients were not permitted to receive any other type of rehabilitation during the period of the study. The study reported that there were no adverse events of either treatment, however there was no information provided regarding safety or tolerability.

In this study, mean values and standard deviation were used as descriptive statistics to measure PDQ-8 scores before and after treatment and the level of significance was established at $p<0.025$ for post hoc analysis.[3] As shown in Table 3, both groups demonstrated an overall improvement in outcomes measured before and after treatment.[3] The TeleWii group had a decrease of 4.9 from a pre-treatment mean of 30.72 to a post-treatment mean of 25.82 ($p<0.001$), while the in-clinic group had a decrease of 6.62 from a pre-treatment mean of 30.53 to a post-treatment mean of 23.91 ($p=0.016$).[3] However, there was no significant between-group difference in PDQ-8 outcomes as measured by the post hoc analysis ($p>0.025$).[3]

Table 3. Mean (SD) Change in QOL and P-Values in a Study Conducted by Gandolfi et al.[3]

	Pre-Intervention Mean (SD)	1 Month Post-Intervention Mean (SD)	Post Hoc Analysis P-Value Within Groups	Post Hoc Analysis P-Value Within Groups
TeleWii**	30.72 (15.54)	25.82 (14.89)	<0.001	>0.025
In-Clinic**	30.53 (16.04)	23.91 (13.20)	0.016	
**For post hoc analysis, p-value <0.025 is significant				

The RCT conducted by Tollar et al. involved patients with a diagnosis of Parkinson's with Hoehn and Yahr stages 2-3.[6] Initially, 72 subjects were found by referrals from neurologists in the area and by calling patients in the hospital's database. Prior to the study, patients were subjected to preliminary screening which included a full neurological examination, a gait and posture examination, and an evaluation of cognitive function. Additionally, participants were instructed to remain on levodopa medication therapy in order to lessen motor symptoms. Patients were excluded if they presented with cognitive deficits, depression, severe cardiovascular disease, uncontrolled DM, history of stroke, traumatic brain injury, seizure disorder, or current involvement in an exercise program or deep brain stimulation. Exclusion criteria was instilled as these factors could have possibly altered motor ability and therefore, response to treatment. Of the 72 eligible participants, three were excluded for reasons stated above and five declined to participate.

The subjects in the study conducted by Tollar et al. were randomly allocated into a no physical intervention control group or a high-intensity agility intervention group.[6] Of the remaining 64 patients who were randomly allocated to either the control or intervention group, 9 patients were excluded as they refused to be tested at baseline and withdrew from the study. Patients in the intervention group underwent 15 one-hour sessions over 3 weeks, which included 4 parts that focused on postural instability and motor deficits: a warm-up, sensorimotor and visuomotor agility training, sensorimotor agility training using virtual reality modules, and a cool-down. These sessions were offered in the hospital's physical therapy gym under supervision of up to 3 physical therapists who implemented strict safety guidelines. Compliance was measured through an attendance and symptom log, which showed 100% adherence to the exercise program. The study did not provide reports on safety, tolerability, or adverse effects.

In this study, the results of the PDQ-39 were reported as mean differences, with a change of 4.7 considered to be clinically significant and a level of clinical significance set at $P<0.05$.[6] As shown in Table 4, the intervention group improved in PDQ-39 outcomes before and after treatment, while the control group did not improve.[6] In the high-intensity agility group, there was a 6.6-point decrease from the pre-intervention score of 30.0 to the post-intervention value of 23.4 ($p<0.001$).[6] In comparison, the control group had a 0.2 increase from the pre-intervention score of 30.6 and a post-intervention score of 30.8 ($p>0.05$).[6] The difference between the mean values of the intervention group before and after treatment was large and exceeded the 4.7-point threshold, indicating a clinically significant reduction in quality of life.

Table 4. Mean (SD) Change in QOL and P-Values in a RCT Conducted by Tollar et al.[6]

Group	Pre-Intervention Mean (SD)	Post-Intervention Mean (SD)	P-Value
Intervention*	30.0 (8.3)	23.4 (7.2)	<0.001
Control	30.6 (15.0)	30.8 (13.8)	>0.05
*P-value <0.05 is significant			

DISCUSSION

The results of this study were conflicting as two studies presented statistically significant results and one study had insignificant results. In the case series by Souza et al., there was no statistical significant reduction in PDQ-39 scores besides in the daily activities domain.[2] However, it has been shown that this specific domain is strongly associated with improving the health of patients with Parkinson's disease.[2] In the RCT by Gandolfi et al., there was no significant change between groups when comparing quality of life scores in the virtual reality balance training to in-clinic balance training, but there were significant changes in the two groups overtime.[3] Nonetheless, this is clinically significant as the quality of life of PD patients can improve regardless of treatment modality. The results of Tollar et al. showed significant improvement in PDQ-39 outcomes in the intervention group, which were attributed to improvement in motor symptoms.[6]

Each study acknowledged various limitations that may have affected the generalizability and significance of the results. In the case series by Souza's et. al, the small sample size, lack of a control group, and great variability in disease stages of the participants may have limited the outcomes of this study.[2] Individuals in early stages of the disease without disabling symptoms had a good perception of their quality of life prior to intervention, which may have limited their ability to achieve significant improvements in their scores after treatment.[2] Limitations in the study conducted by Tollar et al. include lack of follow up post treatment and lack of measurement of physical activity and diet modifications during treatment.[6] Additionally, Tollar et al. proposed that the Hawthorne effect may have swayed the results as participants could have improved just from treatment and close observation.[6]

While virtual reality programs have proven to be feasible and effective in improving postural control, gait, and cognition in several neurological conditions, there are limitations of this treatment. One limitation is the safety of virtual reality programs in patients due to potential hazards of participation.[3] It has been reported that virtual reality can result in adverse symptoms like sickness, dizziness, and headache.[7] Another limitation posed by Tollar et al. are policy issues regarding reimbursement of therapy.[6] Although virtual reality training has been proposed as a cost-effective treatment, the cost of this new technology is high.[7] Further investigation is required to determine the costs associated with this novel rehabilitation program.

CONCLUSION

Based on the results of the two RCTs and one case series reviewed in this study, the evidence is conflicting on whether or not virtual reality therapy is effective in improving quality of life for adults with Parkinson's disease. The case series by Souza et al. did not have significant improvement in scores, which may have been influenced by the limitations of the study.[2] However, in the two RCTs, there was a clinically meaningful reduction in PDQ scores in the virtual reality intervention group, which holds potential for this therapy in the future.[3,6] Further studies are warranted with a larger variety of control groups, larger sample sizes, and longer duration of treatment and follow up. Additionally, future research on treatment safety, adverse effects, and tolerability is critical. As the projected burden of chronic conditions like Parkinson's disease continues to grow, there is an increased need for innovative treatment options to prevent, delay onset, and alleviate symptoms of these conditions. Although virtual reality therapy opens new opportunities for benefiting Parkinson's disease patients, more rigorously designed randomized controlled trials are needed to provide a stronger evidence-based basis to prove the potential advantages.

References

1. Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A. The current and projected economic burden of Parkinson's disease in the United States. *Mov Disord*. 2013;28(3):311-318. https://onlinelibrary.wiley.com/doi/abs/10.1002/mds.25292. doi: 10.1002/mds.25292.

2. Souza, Maria Fernanda da Silva, Bacha JMR, Silva KGd, Freitas TBd, Torriani-Pasin C, Pompeu JE. Effects of virtual rehabilitation on cognition and quality of life of patients with Parkinson's disease. *Fisioterapia em Movimento*. 2018;31. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0103-51502018000100225&lng=en&tlng=en. doi:10.1590/1980-5918.031.ao12.

3. Gandolfi M, Geroin C, Dimitrova E, et al. Virtual reality telerehabilitation for postural instability in Parkinson's disease: a multicenter, single-blind, randomized, controlled trial. *Biomed Res Int*. 2017;2017:7962826.

4. Parkinson's disease. Mayo Clinic Website. https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/diagnosis-treatment/drc-20376062. Updated 2018. Accessed November 31, 2019.

5. Mou L, Ding W, Fernandez-Funez P. Open questions on the nature of Parkinson's disease: From triggers to spreading pathology. *J Med Genet*. 2019:jmedgene-106210. http://jmg.bmj.com/content/early/2019/09/03/jmedgenet-2019-106210.abstract. doi: 10.1136/jmedgenet-2019-106210.

6. Tollár J, Nagy F, Kovács N, Hortobágyi T. A high-intensity multicomponent agility intervention improves parkinson patients' clinical and motor symptoms. *Arch Phys Med Rehabil*. 2018;99(12):247-2484.e1. http://www.sciencedirect.com/science/article/pii/S0003999318303538. doi: //doi.org/10.1016/j.apmr.2018.05.007.

7. Massetti T, da Silva TD, Crocetta TB, et al. The clinical utility of virtual reality in neurorehabilitation: A Systematic Review. *J Cent Nerv Syst Dis*. 2018;10:1179573518813541. Published 2018 Nov 27. doi:10.1177/1179573518813541.